# A randomized, double-blind, placebo-controlled, single ascending dose and multiple dose study to evaluate the safety, tolerability and pharmacokinetics of Cannabidiol (GWP42003-P) oral liquid formulation with an open label two-period cross-over part to study food effects in healthy subjects

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Seizures (incl subtypes) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON42686

**Source**
ToetsingOnline

**Brief title**
Cannabidiol (GWP42003-P) SAD, FE and MD study

### Condition

- Seizures (incl subtypes)

**Synonym**
Epilepsy

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** GW Research Ltd.
**Source(s) of monetary or material Support:** Farmaceutische industrie

## Intervention

**Keyword:** Cannabidiol, Epilepsy

## Outcome measures

### Primary outcome

To evaluate the safety and tolerability of single ascending and multiple doses

of cannabidiol (CBD, GWP42003-P) in healthy male and female subjects compared

with placebo with respect to:

- incidence, type and severity of adverse events (AEs).

- vital signs.

- 12-lead electrocardiogram (ECG).

- clinical laboratory parameters.

- physical examination.

### Secondary outcome

To assess the pharmacokinetics (PK) of single ascending and multiple doses of

CBD (GWP42003-P) in healthy male and female subjects.

To assess the effect of food on the PK of CBD (GWP42003-P) following a single

dose of CBD (GWP42003-P) in healthy male and female subjects.

To assess the changes from baseline in the Cannabis Withdrawal Scale (CWS) score

To assess the changes from baseline in sleep disruption 0-10 Numerical Rating

Scale (NRS) score.

To assess the changes from baseline in Epworth Sleepiness Scale (ESS) score.

To assess the changes from baseline in Columbia Suicide Severity Rating Scale

(C SSRS) questionnaire (multiple dose only)

# Study description

### Background summary

Cannabidiol (CBD) is a new investigational compound that may eventually be used for the treatment of epilepsy. It is extracted from cannabis plants under highly controlled conditions to ensure the product is always the same. Within the human body there is a biological system named the endogenous cannabinoid system (ECS). CBD is absorbed and distributed very rapidly to tissues and a number of the therapeutic actions of CBD are thought to be produced via the body*s own ECS.
CBD is not yet registered as a drug but has been given to humans in both clinical studies and as part of an approved product in combination with another drug in a number of countries.

### Study objective

The purpose of the study is to investigate to what extent CBD is safe and tolerated. It will also be investigated how quickly and to what extent CBD is absorbed and eliminated from the body (this is called pharmacokinetics). Furthermore the effect of food on the pharmacokinetics of CBD will be investigated.This study is not intended to improve the volunteer health, but is necessary for the further development of CBD.

### Study design

The study will be performed in 2 parts (single ascending dose [SAD] part with integrated food effect [FE] part and multiple dose [MD] part).
The study exists of 1 period for the the SAD, 3 periods for the SAD with FE and 1 period for the MD. The volunteers will stay in the clinical research center in Zuidlaren for 4 days (3 nights) in the SAD, for 5 days (4 nights in the FE periods and for 11 days (10 nights) in the MD part.

**Intervention**

The SAD part of the study will consist of 1 study period during which you will receive either CBD or placebo once. CBD and placebo will be given in the form of an oral solution

The FE part of the study will consist of 2 study periods (Study Periods 2 and 3) during which the volunteers will receive CBD, once with a breakfast and once without a breakfast, however the order in which this will occur will be determined by chance. CBD will be given in the form of an oral solution. Thus, participants participating in both the SAD part and FE part will receive the study compound in 3 study periods.

The MD part of study will consist of 1 period during which the volunteers will receive CBD or placebo twice daily for 6 days with a single dose in the morning of day 7. CBD and placebo will be given in the form of an oral solution.

**Study burden and risks**

The following side effects were experienced among a portion of the 213 patients who have taken CBD oral solution; however this was not within a formal clinical study (there was no placebo treatment). All were considered to be caused by the study compound. They have been categorized by the likelihood of them occurring, and listed in the order they have most commonly been reported.
Very common side effects which may affect more than one person in every 10 are: Feeling drunk, sleepy or abnormal, feeling tired, diarrhea and eating less than usual.
Common side effects which may affect more than one person in every 100 are (excluding the very common side effects above): Eating more than usual, weight gain, weight loss, convulsions, difficulty walking and amounts of medicines in the body were higher than usual (increases of levels of other medicines), increased appetite, decreased appetite, feeling drugged.
Some patients have also developed rashes during treatment with CBD oral solution.
The following side effects have been seen in 107 patients who have previously taken other CBD medicines (either CBD botanical drug substance or purified CBD) within clinical studies. It should be noted that 87 of these patients took a formulation containing small amounts of other cannabinoids including tetrahydrocannabinol (THC) and so may have resulted in a higher incidence of side effects than with the study compound you will be using. They have been categorized by the likelihood of them occurring, and listed in the order they have most commonly been reported. A lot of these effects have also been seen with the placebo medication. The side effects in bold have been seen in 20 patients who have previously taken study medication of purified CBD, all being classed as common, with the exceptions of headache and diarrhea which were very

common.

Very common side effects which may affect more than one person in every 10 are: Diarrhea, headache, feeling sick.
Common side effects which may affect more than one person in every 100 are (excluding the very common side effects above): Mouth problems (including, pain, discomfort, change in sense of taste or loss of sense of taste, dry mouth, reduction in or loss of sensation), feeling tired,indigestion, sickness, eating less than usual, feeling drunk or abnormal, feeling dizzy, neck pain, belching, urgency to pass motions, increased frequency in passing water, rashes, change in liver function blood tests or hematology blood tests, cold symptoms, abdominal pain, constipation, feeling depressed or confused, abnormal dreams, nose bleed, feeling weak or unwell, flushing, muscle spasms.
If you suffer from any of the following side effects, you should immediately inform the study doctor about this: Serious allergic reaction, such as a severe rash, swelling in the mouth or throat, tightness in the throat or feeling like the throat or airways are closing, difficulty breathing, severe light-headedness or a faint feeling, or any thoughts of suicide.

Procedures:

Registration of side effects:
During the entire study all side effects you report will be documented.

Blood sampling, indwelling cannula (SAD, FE):
During this study less than 500 milliliters of blood will be drawn.
An indwelling cannula (a needle that is inserted into a vein into the arm) will be used each study period to sample blood on Day 1 (SAD, FE) and on Day 7 (MD) will be removed before you go home. Remaining blood samples between the pre-study screening and the post-study screening will be drawn by direct puncture of the vein.

Vital signs:
Respiratory rate, blood pressure, pulse rate and body temperature will be measured regularly in supine position. Blood pressure and pulse rate will also be measured in standing position.

Heart trace (ECG):
ECGs will be taken regularly.

Meals:
Volunteers will receive a high fat breakfast once during FE

Sleep disruption and Epworth Sleepiness Scale questionnaires:
During the study volunteers will need to complete 2 separate questionnaires to measure sleep disruption during the night and your daytime sleepiness.

Cannabis withdrawal scale:
During the study volunteers will receive a questionnaire to measure any symptoms of withdrawal reactions.

Columbia Suicide Severity Rating Scale:
During the study volunteers will receive a questionnaire to measure any suicide-related thoughts or behaviors.

# Contacts

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**Scientific**
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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

- healthy male/ female subjects
- 18-45 yrs, inclusive

- BMI: 18.0-28.0 kg/m2, inclusive

### Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood (for men) / 1.0 liters of blood (for women) in the 10 months prior the start of this study.

## Study design

### Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 27-05-2015 |
| Enrollment: | 56 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | NA |
| Generic name: | Cannabidiol |

## Ethics review

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| Approved WMO Date: | 20-05-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 27-05-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 03-08-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 10-08-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2015-001754-15-NL |
| CCMO | NL53526.056.15 |